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MARKED-UP VERSION OF THE AMENDMENTS

IN THE CLAIMS:

Claims 1, 20 and 55 have been amended as follows:

1. (Three Times Amended) A method for the prevention or treatment of inflammation or inflammatory-related disorder present in a pathological condition selected from the group consisting of infarct, arthritis, diabetes, artherosclerosis, tumor, hepatitis, infection, and neuro-degenerate diseases, comprising administering to a mammal in need of such treatment a composition comprising total yeast ribonucleic acid and a pharmaceutically acceptable vehicle, carrier, or diluent, said composition comprising said ribonucleic acid in an amount effective to ameliorate symptoms of inflammation or inflammatory-related disorder, wherein said composition is administered so that said ribonucleic acid is present into the mammal's blood.

20. (Four Times Amended) A pharmaceutical composition for the treatment or the prevention of inflammation or inflammatory-related disorder, comprising total yeast ribonucleic acid and a pharmaceutically acceptable vehicle, carrier, or diluent, wherein the composition comprises ~~at least~~ more than 14.5% by weight nitrogen and ~~at least~~ more than 8.5% by weight phosphorus.

55. (Amended) A method for the prevention or treatment of inflammation or inflammatory-related disorder, comprising administering to a mammal in need of such treatment a composition comprising total yeast ribonucleic acid and a pharmaceutically acceptable vehicle, carrier, or diluent, said composition comprising said ribonucleic acid in an amount effective to ameliorate symptoms of inflammation or inflammatory-related disorder,

wherein said composition is administered so that said ribonucleic acid is present into the mammal's blood, and

wherein said ribonucleic acid has a nitrogen content of more than 14.5% by weight and a phosphorus content of more than 8,5% by weight.

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REMARKS

By the present amendment, independent claims 1, 20 and 55 have been amended.

Specifically, claim 1 has been amended to clarify that the method is for the prevention or treatment of inflammation present in the pathological conditions listed in the Markush group. Support for the added recitation is found in the original application, in particular in the first full paragraph of page 54.

Claim 20 has been amended to recite the lower limits of more than 14.5% by weight nitrogen and more than 8.5% by weight phosphorus, as recited in present claim 55.

Claim 55 has been amended to present "wherein" clauses in separate paragraphs.

As a preliminary, Applicant and Applicant's representative thank the Examiner for allowing an opportunity to discuss the case and file a supplemental response.

In addition to the remarks set forth in the response filed on September 25, 2002, the following comments are submitted.

CLAIM 1

Enablement

Claim 1 is directed to a method for the prevention or treatment of inflammation or inflammatory-related disorder, in which the inflammation is present in the pathological conditions listed in the Markush group, which are all non-wound-related conditions. It is noted that claim 1 is not directed per se to a method of preventing or treating the listed conditions, but to a method

of preventing or treating inflammation or inflammatory-related disorder present in these conditions. Extensive evidence has been submitted in previous responses (in particular the response filed on May 2, 2002) to show that the experiments reported in the present specification are sufficient to establish the effectiveness of the composition against inflammatory processes.

Novelty over Kulkarni

Claim 1 is directed to a method comprising administering yeast RNA to prevent or treat an inflammatory process in connection with only non-wound-related conditions, according to the definition of a wound in Kulkarni. Therefore, claim 1 is not anticipated by Kulkarni.

Non-obviousness over combinations of references including Kulkarni

In addition, Kulkarni discloses administering nucleotides, including RNA, to promote wound healing by promoting collagen repair. However, even though Kulkarni mentions in its introduction the presence of inflammations as a first stage, Kulkarni is silent as to any effect of RNA on inflammatory processes. Therefore, Kulkarni fails to teach or suggest administering RNA to address inflammations, so that present claim 1 is not obvious over Kulkarni or any combination of the cited references including Kulkarni.

CLAIM 55

Non-obviousness over combinations of references including Kulkarni of yeast RNA purification to improve nitrogen and/or phosphorus contents

Claim 55 is directed to a method for the prevention or treatment of inflammation or inflammatory disorder using a composition containing total yeast ribonucleic acid having a nitrogen content of more than 14.5% by weight and a phosphorus content of more than 8,5% by weight. These nitrogen and phosphorus contents are not present in the yeast RNA administered by Kulkarni to promote wound repair. Specifically, Kulkarni does not specify nitrogen or phosphorus content, but Kulkarni does not provide any motivation to modify its yeast RNA to increase nitrogen and/or phosphorus content, such as by removing residual DNA. Thus, a person of ordinary skill in the art would use a simple extraction process, which would result in a yeast RNA product having a low nitrogen and phosphorus content as shown on page 26 of the present specification (first stage of the extraction process, as described in the first four lines of the paragraph). Even if, arguendo, a person of the art had looked into the literature for alternative yeast RNA products, the highest values mentioned in the literature are 15.1% nitrogen and 8.5% phosphorus in Ayukawa for a product intended for the food industry, which is still below the claimed ranges. Thus, a person of the art would have had no motivation or suggestion to further modify the yeast RNA to increase nitrogen and/or phosphorus contents.

Unexpected results

In addition, Kulkarni is not interested in the nitrogen and/or phosphorus contents of its yeast RNA product but is concerned only about the overall nucleotide content (see col. 13, lines 35-37: "Yeast RNA is employed as an example of the particular nucleotides that may be employed in the practice of the present invention"). In contrast, the present inventor has found that, by increasing the nitrogen and phosphorus contents of the yeast RNA composition, it is possible to obtain considerably improved effects on inflammatory processes. Clear evidence of these unexpectedly improved results is provided in the present specification and is extensively discussed in the response filed on September 25, 2002. These improvements in the activity of yeast RNA against inflammatory processes is totally unexpected since Kulkarni does not even mention any activity of yeast RNA against inflammation. Therefore, present claim 55 is not obvious over Kulkarni or any combination of the cited references including Kulkarni.

CLAIM 20

Non-obviousness over combinations of references including Iyer and/or Ayukawa

Claim 20 is directed to a composition for the prevention or treatment of inflammation or inflammatory-related disorder comprising more than 14.5% by weight nitrogen and more than 8.5% by weight phosphorus. This higher nitrogen and phosphorus contents are obtained for example by the extraction process described on page 26 of the present specification, i.e., by successive

purification cycles until the desired nitrogen and/or phosphorus contents are obtained (see Table 1 on page 27 of the present specification).

Iyer discloses only a simple extraction process involving only one washing, drying and resuspension cycle (see Iyer on page 5209, left col., middle of the second paragraph). Therefore, the extraction process of Iyer corresponds to the first step of the process described on page 26 of the present specification, and results in a much lower nitrogen and phosphorus content than the values required by present claim 20. Since Iyer is satisfied with its yeast RNA product for its hybridization purposes, Iyer does not provide any motivation for further modification.

Further, as discussed above, Ayukawa also fails to disclose further modification of its product.

In contrast, as discussed above, the present inventor has shown unexpectedly improved effectiveness of a yeast RNA composition when nitrogen and phosphorus content are increased. Therefore, present claim 20 is not obvious over Iyer, Ayukawa, or any combinations of the cited references including these references.

Non-obviousness over combinations of references including Kulkarni

The nitrogen and phosphorus contents recited in claim 20 are the same as recited in claim 55. Thus, the same remarks above with respect to claim 55 also apply to claim 20. Kulkarni fails to provide a motivation or suggestion to purify its yeast RNA product because Kulkarni is concerned only about the total nucleotide content in order to promote collagen repair in a wound. In contrast, the present inventor has established that a yeast RNA composition having higher

nitrogen and/or phosphorus contents considerably improve effectiveness against inflammatory processes. This improved effectiveness is totally unexpected in view of Kulkarni, and therefore, present claim 20 is not obvious over Kulkarni.

Note on "purification of old product"

Reference is made to MPEP 2144.04, heading "Purifying an Old Product" where it is indicated that mere purity of a product, by itself, does not render the product unobvious. It is submitted that the present case is not a "mere purity" case but the case of a modification of a product's composition which provides unexpected results: specifically, a modification of nitrogen and/or phosphorus contents which unexpectedly improves the effect against inflammation.

In Ex parte Gray, 10 USPQ2d (Bd. Pat. App. & Inter. 1989) cited in that section of MPEP, the applicants claimed a purified human protein obtained by recombinant technology. The claims were rejected because the applicants could not demonstrate that the recombinant protein had unexpected properties, as compared to the human protein obtained from a human body. The Board noted that the burden was on applicants to show unexpected properties of the claimed product.

In contrast, in In re Cofer, 148 USPQ 268 (CCPA 1966), also cited in MPEP, the CCPA reversed a determination that claims directed to the free-flowing crystalline form of a compound were unpatentable over the viscous form of the same compound. The CCPA held the claims patentable because the prior art did not suggest the crystalline form or how to obtain such form.

The present invention is unlike the claimed product in Ex parte Gray because, here, applicant has shown an unexpected result of modifying the nitrogen and/or phosphorus content of the yeast RNA composition (i.e., improved effect against inflammation). Rather, the present invention is closer to the situation in In re Cofer, because, like the inventor in In re Cofer, the present inventor has modified the form of the yeast RNA composition in a way that is not suggested in the prior art, and has obtained a different composition having different, and unexpectedly improved, properties. Therefore, the presently claimed composition is not a mere purification of an old product but a composition in a modified form having modified properties, none of which are suggested in the cited prior art.

In view of the above, it is submitted that the prior art rejections should be withdrawn.

In conclusion, the invention as presently claimed is patentable. It is believed that the claims are in allowable condition and a notice to that effect is earnestly requested.

In the event there is, in the Examiner's opinion, any outstanding issue and such issue may be resolved by means of a telephone interview, the Examiner is respectfully requested to contact the undersigned attorney at the telephone number listed below.

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In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of the response period. Please charge the fee for such extension and any other fees which may be required to our Deposit Account No. 01-2340.

Respectfully submitted,

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